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제왕절개 반흔 임신의 성공적인 보존적 치료 4예

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Successful Conservative Management of Cesarean Section Scar Pregnancy

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A Cesarean section scar pregnancy is a rare but possibly life-threatening condition. The diagnosis is made mainly based on transvaginal ultrasonography. We used the Doppler and serial βHCG in determining the severity and prognosis. Because of the rarity, universal treatment has not been established. In our cases, the severity of bleeding was independent of the level of βHCG and the duration of amenorrhea. The shorter the interval from the previous cesarean section, the more severe the symptom, in such case, we were able to preserve fertility by uterine artery embolization. Cesarean section scar pregnancy can be managed conservatively with methotrexate injection. Based on our case review, we can conclude that it is very important that we choose the each therapeutic management based on her history and condition. In our review, we present four cases diagnosed with Cesarean section scar pregnancy all managed conservatively to preserve future fertility.

Key Words: Cesarean Section Scar, Ectopic Pregnancy, Conservative Management

INTRODUCTION

Implantation of pregnancy within a cesarean section scar is considered to be the rarest form of ectopic pregnancy and it was first reported by Larsen and Soloman in 1978.[1-3] But this is possibly life-threatening condition because of the risk of uterine rupture and massive hemorrhage. Since the advent of trans-vaginal ultrasound, the condition, which can be diagnosed earlier and treated more conservatively and then we can avoid hysterectomy and maintain fertility. Because of the different condition of the tubal pregnancy and cervical pregnancy, the treatment modalities should be considered in different way. We report 4 cases of ectopic pregnancy in a cesarean scar diagnosed by transvaginal ultrasound and treated conservatively between the year of 2004 to 2005.

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CASE REPORT

1. CASE 1

A 30-year-old gravida 5, para 2, Rh-positive woman was referred to us under the impression of cervical pregnancy. She presented with heavy vaginal bleeding for one day, after 5^{+5} weeks of amenorrhea. She had undergone a second cesarean delivery at term 5 years earlier and dilatation and evacuation 4 years earlier. Her past medico-surgical history was unremarkable. Physical examination was unremarkable except for moderate bleeding from the external cervical os. Her pulse and blood pressure were normal. Laboratory data revealed a quantitative serum βHCG level of 14864 mIU/mL. Transvaginal ultrasonography demonstrated about 2.5 cm sized heterogenous echogenic mass on the cesarean section scar surrounded by thin myometrium below the urinary bladder. Neither embryonic pole nor fetal cardiac activity was detected. The uterine cavity was empty. No fluid was seen in the cul-de-sac. Based on the ultrasound findings, the diagnosis of cesarean scar pregnancy was made (Fig. 1). Management options were explained to the patient. After discussion, the patient underwent uterine artery embolization in an attempt to decrease the known risk of continuous vaginal bleeding with cesarean scar pregnancy. On day 3, no remarkable bleeding was observed after the intervention. Serum βHCG level was 7216 mIU/mL. Ultrasound-guided transcervical aspiration was performed with a 22 gauge spinal needle. Gestational sac contents were aspirated. A single 50-mg dose of methotrexate (MTX) was injected via intra-sac and no active hemorrhage from the cervical cavity was observed.

Fig. 1. Gestational sac at previous Cesarean section scar.

On day 10, serum βHCG level was 9184 mIU/mL and transvaginal sonography showed slightly enlarged uterus with about 2.7 cm sized heterogenous echogenic mass on the cesarean section scar. Despite the intervention, serum β HCG level, the size of heterogenous echogenic mass and A-V (Arterio-venous) malformation pattern increased. On day 20, she was admitted for treatment and surveillance. Serum βHCG level was 3986 mIU/mL and ultrasonography showed a persistent mass on the section scar. Doppler evaluation revealed increased A-V malformation (Fig. 2). MTX 1 mg/kg (68 kg, 6.8 mg) and leukovorin 0.1 mg/kg for 8 days were administered alternately via IM (intra-muscular). Liver and renal function was regularly checked. No adverse effect of methotrexate was noted.

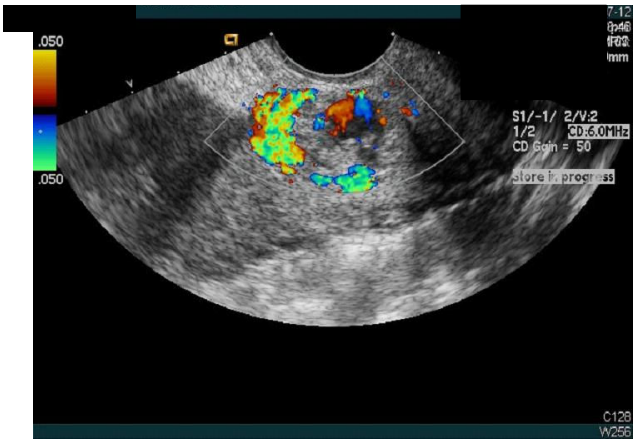

Fig. 2. Doppler ultrasongography shows increased A-V malformation.

On day 27, serum βHCG level was 2320 mIU/mL. On day 32, she presented to the emergency room complaining of persistent vaginal bleeding. Initial vital sign was stable and serum βHCG level was 574 mIU/mL. Transvaginal sonography showed persistent mass on cesarean scar but its location was closer to the lower portion with decreased blood flow compared to previous findings. On day 34, dilatation and evacuation was performed in an attempt to decrease intrauterine content. Serum βHCG level was 62 mIU/mL. On day 49, serum β HCG taken during a routine follow up at our out patient clinic was undetectable and transvaginal sonographic findings was also unremarkable.

2. CASE 2

A 38-year-old gravida 5, para 2, Rh-positive woman was presented to us with heavy vaginal bleeding after 11^{+0} weeks of amenorrhea. Therapeutic dilatation and evacuation had been performed under the impression of partial mole at a private clinic. Four years earlier she had undergone a lower segment transverse cesarean delivery at term. She had 2 prior history of dilatation and curettage. Her past medico-surgical history was unremarkable. Her general physical condition was normal and her vital signs were stable. Gynecologic examination revealed moderate vaginal bleeding. The serum βHCG level was 1834 mIU/mL. Transvaginal ultrasonography showed about 2.6×2.3 cm sized heterogenous echogenic mass on the cesarean scar lesion surrounded by thin endometrium. Neither embryonic pole nor fetal cardiac activity was detected. The uterine cavity was empty. No fluid was seen in the cul-de-sac. Based upon the ultrasound findings, the diagnosis of cesarean scar pregnancy was made (Fig. 3). Uterine artery embolization was performed in an attempt to decrease the known high risk of hemorrhage with cesarean scar pregnancy. The vital signs became stable and vaginal bleeding decreased progressively. On day 2, transvaginal ultrasonography showed persistent mass lesion and about 3.7×3 cm sized right ovarian cyst. On day 10, serum βHCG was 694.8 mIU/mL and transvaginal ultrasonography revealed decreased mass size and persistent right ovarian cyst. On day 14, she presented with moderate vaginal bleeding. General physical examination was normal and her vital signs were stable. Gynecologic examination revealed mild bleeding from cervical os. Serum βHCG level was 244.7 mIU/mL and transvaginal ultrasonography showed about 2.3×2.3 cm sized heterogenous echogenic mass on the cesarean section scar surrounded by thin endometrium. A-V malformation pattern decreased. After discussing the best treatment modality forr this patient, conservative management with rectal cytotec and intravenous oxytocin infusion was chosen because

patient's symptoms were mild. Blood loss was replaced with 2 units of packed RBC. She was discharged from our institution because she was clinically stable. On day 22, serum βHCG taken in our out patient clinic was 90.7 mIU/mL and transvaginal ultrasonography showed no interval change of previous findings. On day 31, serum β HCG level was 2.1 mIU/mL and transvaginal ultrasonography revealed decreased hypoechoic mass of 1.8 cm on anterior wall and the same sized right ovarian cyst. The margin was well demarcated. On day 87, Doppler revealed no abnormal findings (Fig. 4).

3. CASE 3

A 38-year-old gravida 6, para 2, Rh-positive woman was referred to us under the impression of cervical pregnancy from a private clinic with 5^{+6} weeks of amenorrhea. Ten years earlier she had undergone a lower segment transverse cesarean delivery at term. She had 3 prior histories of dilatation and curettage. Her past medico-surgical history was unremarkable. Her general physical condition was normal and her vital signs were stable. Gynecologic examination was unremarkable. The initial serum βHCG level was 27838 mIU/mL. Transvaginal ultrasonography showed about 0.8 cm sized gestational sac including 0.3 cm sized crown-rump, yolk sac, and fetal cardiac activity (112 bpm) on the cesarean scar lesion. The uterine cavity was empty (Fig. 5). No fluid was seen in the cul-de-sac. Based upon the ultrasound findings, the diagnosis of cesarean scar pregnancy was made. MTX 1 mg/kg (75 kg, 75 mg) and leukovorin 0.1 mg/kg were administered for 8 days alternately via IM. Liver and renal function was regularly checked. No adverse effect of MTX was noted. On day 8, serum βHCG level was 36108 mIU/mL and disrupted G-sac was revealed on transvaginal ultrasonography. On day 15, serum β HCG level was 17713 mIU/mL and transvaginal ultrasonography showed disrupted G-sac and loss of fetal cardiac activity. The serial transvaginal ultrasonography showed no interval change on days 23 and 30. On day 32, despite the declining values of serum βHCG, the gestational sac diameter remained the same. Conservative

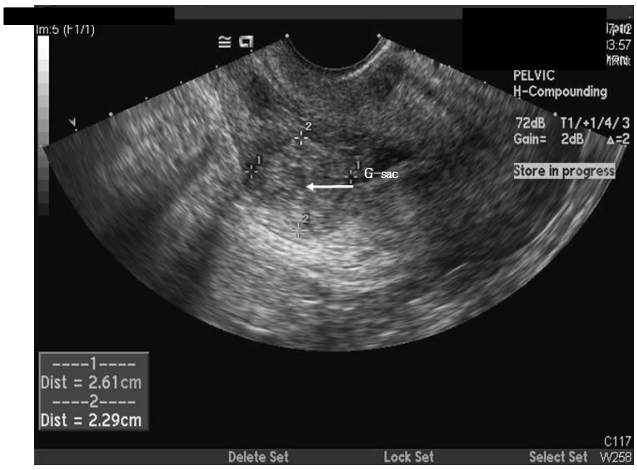

Fig. 3. Gestational sac at previous Casarean section scar.

Fig. 4. Doppler ultrasonography shows no abnormal ffindings.

Fig. 5. Gestational sac at previous Cesarean section scar.

management with single dose of MTX 50 mg/m^2 (50 mg×1.82, 90 mg) was administered intramuscularily. No adverse effect of MTX was noted. She was discharged from our institution because she was clinically stable . Serial serum βHCG level were 554 mIU/mL, 490 mIU/mL, 58 mIU/mL, and 15.6 mIU/mL on days 36, 39, 42, 63 and 98 respectively.

4. CASE 4

A 41-year-old gravida 4, para 2, Rh-positive woman was referred to us from a private clinic under the impression of cervical pregnancy after 6^{+0} weeks of amenorrhea. Her initial presenting symptom was heavy vaginal bleeding. Twelve years earlier she had undergone a second lower segment transverse cesarean deliveries at term. She had a prior history of dilatation and curettage. Her past medico-surgical history was unremarkable. Her general physical condition was normal and her vital signs were stable. Gynecologic examination revealed moderate vaginal bleeding. The initial serum βHCG level was 11447 mIU/mL and transvaginal ultrasonography showed about 0.8 cm sized gestational sac including about 0.2 cm sized yolk sac on the cesarean scar lesion surrounded by thin endometrium.. The uterine cavity was empty. No fluid was seen in the cul-de-sac. Based upon the ultrasound findings, the diagnosis of cesarean scar pregnancy was made. MTX 1 mg/kg and leukovorin 0.1 mg/kg were administered for 8 days alternately via IM. Liver and renal function was regularly checked. No adverse effect of MTX was noted. On the day 7, serum βHCG level was 32925 mIU/mL and transvaginal ultrasonography showed about 1.4 cm sized gestational sac with about 0.4 cm sized yolk sac. We decided to discharge her and have her visit our out patient clinic on regular basis for routine follow up since she was clinically stable with declining βHCG values. On day 14, serum βHCG level was 16697 mIU/mL and transvaginal ultrasonography showed no interval change. The serial serum βHCG level were 7168 mIU/mL, 4633 mIU/mL, 2901 mIU/mL, 2232 mIU/mL, 1705 mIU/mL, 642 mIU/mL, 107 mIU/mL, and 9.5 mIU/mL on the days 21, 25, 28, 35, 42, 49, 63 and 87, respectively. On day 136, serum βHCG level was below 2.0 mIU/mL and transvaginal ultrasonography showed no remarkable findings other than minimal fluid collection in the endometrium.

DISCUSSION

Based on previous case reports, initial presenting symptoms of cesarean scar pregnancies are acute abdominal pain and hypovolemic shock due to massive and life threatening internal hemorrhage (Table 1). Findings from life-saving laparotomy include a sacculus of a ruptured

uterus.[4] The natural history of the cesarean scar pregnancy is unknown since so few cases have been reported in the literature. However, the cesarean scar pregnancies are more common these days, which may reflect the increasing number of assisted reproduction. Trauma and scarring in the endo- and myometrium can occur after cesarean section, dilatation and curettage, myomectomy, operative hysteroscope and manual removal of placenta, which can create a favorable implantation site in that area.[5,6] Formation of a microscopic dehiscent tract in the myometrium after trauma to the uterus is one of the possible pathogenesis for cesarean scar pregnancies but other contributional factors need to be further examined.[7]

Clinical diagnosis of an early pregnancy implanted in a previous cesarean scar is very difficult and need to be differentiated from cervical pregnancy, cervicoisthmic pregnancy, spontaneous abortion in progress and molar pregnancy.[8] The most important diagnostic tool is transvaginal ultrasonography. Vial et al. suggested the three most common sonographic

Table 1. Summary for our cases

	Age	Presenting symptoms	No. of Admission	βHCG (initial)	US findings (initial)	Duration of amenorrhea	Last cesarean section delivery/ No. of cesarean section	No. of [1)]MTX use	No. of [2)]UAE	No. of D&E	Uterus preserved	Interval (days) from first to last visit
Case 1	30	[3)]VB	[4)]3	14864	2.5 cm sized mass FHB(-)	5^{+5}	4 [5)]YA/2	[6)]2	1	1	Yes	49 days
Case 2	38	VB	[7)]2	1834	2.6 cm sized mass FHB(-)	[8)]11^{+0}	4 YA/2	-	1	-	Yes	31 days
Case 3	38	VB	[9)]2	27838	0.8 cm sized mass FHB(+)	5^{+6}	10 YA/2	[10)]2	-	-	Yes	98 days
Case 4	41	VB	1	11447	0.7 cm sized mass FHB(-)	6^{+0}	12 YA/2	1	-	-	Yes	136 days

1) MTX: Methotrexate
2) UAE: uterine artery embolization
3) VB: vaginal bleeding
4) Readmission after 10 days and 32 days respectively due to recurrent bleeding
5) YA: year ago
6) intra sac single dose injection
7) Readmission after 14 days respectively due to recurrent bleeding
8) D&E was performed under the impression of partial mole at a private clinic (amenorrhea 6 weeks)
9) Readmission after 32 days for MTX treatment
10) systemic single dose injection

findings to be i) the implantation of trophoblastic tissue between the bladder and the anterior uterine wall, ii) no fetal contents in the uterine cavity, iii) discontinuity of the anterior wall of the uterus from the sagittal view. If these criteria are not enough in diagnosing cesarean scar pregnancy, Magnetic resonance imaging (MRI) can be effective.[9] In addition, a prominent peritrophoblastic flow due to neovascularization by ultrasound Doppler imaging can be helpful.[10,11] Based on our case reviews, there are no significant relationship among the Doppler imaging and the level of HCG with the prognosis and severity of the disease. However, it is somewhat premature to determine and conclude the significance based on few case reviews and further studies are needed. As the pregnancy progress, the risk of uterine rupture and life-threatening hemorrhage increase and therefore termination of pregnancy must be recommended to the patient. Two principle management options may be considered, medical or surgical. The surgical approach includes wedge excision and evacuation of the gestational sac by laparotomy and minilaparotomy and repair of the cesarean section scar. However, often times, loss of reproduction can result if hysterectomy is performed due to massive bleeding from the implantation site. Medical treatment is the treatment of choice if the patient is hemodynamically stable and when the patient desires to retain her fertility. According to prior studies, initial treatment with MTX is effective in 80% of the cases.[12] MTX can be administered either systemically or locally, however, direct local injection of MTX into the gestational sac may technically be difficult and often times rupture of the uterus and heavy bleeding may follow. However, since the incidence of cesarean scar pregnancy is rare, the best management option, either surgical or medical, is yet to be determined.

After systemic MTX administration, the formation of connection of the chorion to the cavum uteri is considered to be the natural history of cesarean scar pregnancy.[2] If vaginal bleeding occurs after systemic MTX administration, it is important to confirm the formation of this connection by transvaginal ultrasonography or MRI. Additional systemic MTX or dilatation and curettage should be considered to remove this connection of the chorion to the cavum uteri.

Based on our case review, it seems the duration between the last cesarean delivery and the onset of symptoms such as vaginal bleeding is important in terms of recurrence and the severity of bleeding. In two cases, bleeding severe enough to require uterine artery embolization was more frequent when the interval between the last cesarean delivery and the onset of symptoms were shorter (4 years vs. 10,12 years). In this case review, there was no significant relationship among the duration of amenorrhea, the number of cesarean section the patient has undergone, initial serum hCG level, ultrasound findings and the severity of bleeding and recurrence.[13] However, further review and evaluation of similar cases are needed to discuss the relationships between the several factors mentioned above.

It took, on average, about 30-70 days for serum hCG level to decline below 60 mIU/mL after symptoms resolved, which is comparable to previous case reports. Similar to previous case reports, most of our patients were conservatively managed with MTX (Table 2).

Based on our experience, we think that

Table 2. Summary for previous cases

	Age	Presenting symptoms	βHCG (initial)	US findings (initial)	Duration of amenorrhea	Last cesarean section delivery/ No. of cesarean section	No. of [1]MTX use	No. of [2]UAE	No. of D&E	Uterus preserved	Interval (days) from first to last visit
M. Arslan et al	32	Nausea Vomiting	>10000	3.5 mm mass FHB(+)	7	3 [3]YA/?	−	−	1	Yes	90 days
Min M. Chou et al	26	[4]VB	6413	4 cm sized mass Neovascularization	8	?/1	1	2	−	Yes	120 days
Michael T. et al	21	Abortion	21866	3.3 cm sized mass FHB(+)	8	5 [5]MA/?	1	−	−	Hysterotomy with uterine preservation	F/u loss
Jesse Chuang et al	40	VB	7052	Scar pregnancy	?	?/1	1	−	−	Vasopressin injection to G-sac	30 days
Olivier Graesslin et al	34	Abdominal pain	9585	2.3 cm sized mass FHB(+)	6	3YA/?	1	−	−	Yes	40 days
Frank Nawroth et al	31	Asymptomatic Amenorrhea	45774	6.0×4.3 cm sized mass Strong circular perfusion	8^{+3}	?/?	1 intra+IM	−	−	Yes	97 days
Pierre-Arnaud Godin et al	33	VB	62000	Implanted GS on scar	6^{+3}	?/2	1 direct injection + KCl	−	−	Yes	82 days

[1] MTX: Methotrexate
[2] UAE: uterine artery embolization
[3] YA: year ago
[4] VB: vaginal bleeding
[5] MA: month ago

treatment for cesarean section scar pregnancy should be similar to that of tubal pregnancy.[14] The pathogenesis, clinical manifestations, and imaging studies of cesarean scar pregnancy and cervical pregnancy are similar. However, in terms of treatment, cesarean scar pregnancy should be managed similar to that of tubal pregnancy. The gestational sac of cervical pregnancy is located in the fibrous wall of cervix where muscle is scarce and the only surgical option is hysterectomy because wedge resection could lead to life threatening bleeding.[12,14] However, wedge resection of the gestational sac and repair of the fibrous scar tissue in cesarean section scar pregnancies is proven to be more effective based on previous case reports.[3,8]

In all 4 cases, patients were managed expectantly without surgical intervention. However, in some cases recurrent vaginal bleeding occurred after expectant management and required either uterine artery embolization[15] and MTX treatment which were both costly and time consuming.[16-19] From our experience, surgical removal of the gestational sac and repair of the fibrous scar tissue may help avoid such complications and recurrence in the future. However, because the implant may occur in the vesico-uterine space of the bladder wall and the cesarean section scar is surrounded by dense fibrous scar tissue, injury to the surrounding anatomy may occur. Thus, no single treatment modality is entirely reliable and thus treatment options should be based on each patient's circumstances.[19,20]

Implantation of a pregnancy within a cesarean section scar is rare and further case review and research is needed. Current diagnostic tools enable us to make an early detection of cesarean section scar pregnancies and differentiate it from other forms of ectopic pregnancies. Because of the rarity of these cases, no universal treatment plan has been established. Early detection and treatment is important, however, further effort is needed to establish the risk factors and focus on reducing the number of cesarean section scar pregnancies from occurring in the first place.

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= 국문초록 =

제왕절개 반흔 임신은 매우 드문 질환이지만 생명을 위협하는 치명적인 질환이기도 하다. 본 질환은 주로 질식 초음파를 통해서 진단한다. 본 연구에서 질환의 정도나 예후결정에 도플러 초음파와 연속적인 βHCG값의 측정을 이용하였다. 본 질환은 흔하지 않은 특성으로 인해, 보편적인 치료방법은 아직까지 정립되어있지 않다. 금번 연구에서 이상 질출혈의 정도는 βHCG값이나 무월경 기간과는 무관하였다. 증상의 발현과 이전의 제왕절개 기간이 짧을수록 증상은 더욱 심하였으며, 이런 경우 자궁 동맥 색전술로 임신력을 보존할 수 있었다. 제왕절개 반흔 임신은 보존적으로 methotrexate 항암요법으로 치료될 수 있었다. 본 연구에서 환자의 과거력과 현재의 상태에 따른 각각의 치료방법을 선택하는 것이 중요하다는 결론을 얻을 수 있었다. 이에 추후의 임신력을 유지하면서 성공적인 보존적 치료가 되었던 제왕절개 반흔 임신의 치료 4예를 보고하는 바이다.

중심단어: 제왕절개 반흔, 자궁외 임신, 보존적 치료